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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/700,259	10/30/2001	Geoffrey P. Margison	PM 275388	3434

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/700,259	MARGISON ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *29-31,33,49 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28,30,32 and 34-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 November 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This Action is in response to the communication filed on 1/7/04. Claims 1-50 are currently pending in the application and are addressed herein.

Election/Restrictions

2. Applicant's election without traverse of group I (claims 1-48, as well as the following species: HSV-TK, GM-CSF, radiation in the form of subatomic molecules, and cyclophosphamide) in Paper filed 1/7/04 is acknowledged.

3. Claims 49 and 50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, claims 29-31 and 33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. It is noted that the restriction requirement did not acknowledge claim 50; however, claim 50 is drawn to a method for treating tumor cells, which is encompassed by Group II (claim 49). As such, claim 50 is joined to Group II, which is hereby withdrawn from consideration for the reasons set forth herein. Election was made **without** traverse in the Paper filed 1/7/04. Claims 1-28 and 32-48 are examined herein.

Claim Rejections - 35 USC § 112, second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-28 and 32-48 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to "Vector material" characterized in that said material contains: (a) a tumor cell sensitizing gene; (b) a sensitizing gene expression regulatory system; (c) at least one control gene; and (d) a control gene expression regulatory system, as indicated in claim 1. It is noted that the term "vector material" is not expressly defined in the specification. As such, it is indefinite what the term "vector material" encompasses. That is, it is unclear, without an explicit definition of "vector material" if an expression vector can be considered "vector material" or if merely capsid protein from a viral vector can be considered "vector material". It is noted that vector material is not a readily apparent art-recognized term, considering the claim as a whole. Amending the claim to "a composition comprising" rather than "vector material"; or, alternatively, amending the claim to "An expression vector comprising" rather than "vector material" would obviate this rejection. It is noted that all examined claims depend on claim 1, and therefore, all claims are rejected for depending on the rejected claim.

6. Claim 32 recites the limitation "the antitumor drug" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-28 and 32-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

9. It noted that the specification appears to describe the gene regulatory system such that the system may be comprised on one or two different expression vectors. Should applicants wish to pursue the gene regulatory system described in the specification, applicants should amend the claims and clearly distinguish the gene regulatory system consisting of a single expression vector and the gene regulatory system consisting of two expression vectors.

10. It is noted that although the claims are indefinite, it appears that the claims encompass a gene expression regulatory system comprising a dual layer control mechanism. The dual layer control mechanism appears to comprise: 1) a control gene expression regulatory system that expresses a control gene wherein the regulatory system is responsive to "an expression inducing influence", and 2) a sensitizing gene regulatory system that expresses an antitumor gene wherein the sensitizing gene regulatory system is responsive to a control gene. It is noted that the 2 elements are linked by the expression of the control gene. However, the claims are very broad and encompass possible a huge number of different "expression inducing influences"; a huge number of different control genes, considering every possible influence and control encompassed by the claims, including things which have yet to be discovered.

11. Furthermore, claim 1 encompasses a "control gene regulatory system" (see claim 1-(d)) wherein the control gene regulatory system is responsive in use in a transfected cell to the effect

of a predetermined exogenous or endogenous expression inducing influence so as to induce expression of said control gene to yield an expression product having a capacity to establish an operative linkage between said sensitizing gene expression regulatory system and said sensitizing gene or genes effective to trigger and switch on or permit continuous or permanent expression of the later to bring about continuous production of said sensitizing gene expression product (see claim 1). It is respectfully pointed out that there is no description of the structure of the "control gene regulatory system". The limitations described in claim 1, with respect to the control gene regulatory system, are merely functional limitations indicating what the control gene regulatory system does.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant identifying characteristics (i.e. structure or other physical and/or other chemical properties), by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (See MPEP 2100-164)

However, in the instant case there is no description of any relevant identifying characteristics such as structural elements common to the members of the genus, nor is there any description of the functional characteristics coupled to a correlation between structure and function (i.e., no structure/function relationship has been disclosed), nor is there any description of the identifying structural characteristics sufficient to show that applicant was in possession of

the claimed genus. It is noted that all examined claims depend on claim 1, and as such, all claims are rejected for the same reasons.

12. Claim 1 also encompasses "a predetermined exogenous or endogenous expression inducing **influence**" (see claim 1-(d), emphasis added). Considering that the claims can be interpreted in the broadest reasonable interpretation, an expression inducing influence encompass influences that can be due to material elements or non-material (e.g., intangible) elements. With respect to material elements that have an expression inducing influence, it is noted that there are a number of different material elements that are described and recognized in the art that have an influence on gene expression, these elements include proteins such as transcription factors and hormones, chemicals such as cyclohexamide, as well as other materials such as radiation, which can indirectly activate expression by causing DNA damage that activates DNA repair proteins synthesis via activation of transcription factors. However, the claims also encompass non-material factors that can influence gene expression. It is noted that non-material factors includes all non-material elements, such as emotions, thoughts, ideas, etc. The specification and relevant prior art does not describe any non-material factors which can influence gene expression. Considering the guidelines indicated above in view of the description present in the instant application and in the prior art, there is insufficient description of the non-material factors that can influence gene expression.

13. Claim 1 also encompasses a huge number of control genes, considering all the possible control genes encompassed by the claims, including those that have not yet been identified. It is noted that the control gene must be able to affect the sensitizing gene expression regulatory system such that expression of the control gene results in the continuous or permanent expression

of the tumor sensitizing gene (e.g., antitumor gene); (see claim 1(d)). Looking to the specification, for a description of the control genes, it appears that the only control genes which could have the desired effect that are described in the specification are control genes that express recombinase enzymes (e.g., Cre or Flp) and promoter-specific transcription factors that specifically activate the expression of genes that are in operable linkage with the target promoter. However, as discussed above, the claims encompass any control gene, including control genes that are not recombinase enzymes and which are not transcription factors and which are structurally and functionally distinct from the described control genes. Considering the guidelines indicated above in view of the description present in the instant application and in the prior art, there is insufficient description of the control genes encompassed by the claims.

14. Additionally, claims 1-28 and 32-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, in view of the written description rejection above. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As mentioned above, the claims encompass a control gene regulatory system and a predetermined exogenous or endogenous expression inducing influence(s) and control gene(s) for which there is insufficient written description provided. Without a clear indication of the structure of the elements that comprise the control gene regulatory system and the predetermined influence and specific control genes encompassed by the claims, one of skill in the art would not know how to make or use the claimed invention without performing an undue amount of additional experimentation.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 1, 5, 6, 8, 11, 14, 16, 23, 24, 41, 44, 45, 46 rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,120,764 (Graham et al.).

It is noted that although claim 1 is indefinite because the term "vector material" is not defined, the instant rejection is applicable in view of the interpretation that "vector material" is an expression vector, or a composition comprising one or more expression vectors.

The instant claims is very broad and encompasses a composition comprising: (a) a tumor cell sensitizing gene, (b) a sensitizing gene expression system, (c) at least one control gene, and (d) a control gene regulatory system. It is noted that the tumor cell sensitizing gene can be any gene that has the potential to cause tumor cells to be killed, a sensitizing gene regulatory system encompasses any system for regulating the expression of the sensitizing gene, a control gene can be any gene that regulates the sensitizing gene regulatory system, and the control gene regulatory system can be any system that regulates the expression of the control gene and thus, in turn, regulates the expression of the sensitizing gene.

Graham teaches a composition comprising adenoviral vectors that comprise a gene regulatory system wherein the gene regulatory system effects the expression a control gene (the

control gene being the cre gene) (e.g., see abstract; Figure 9; column 2, lines 8-45; column 4, line 54 through column 8; column 16, line 1 through column 17 line 52). The expression of the cre gene then regulates the expression of a tumor cell sensitizing gene (the p53 gene) by causing a recombination (via loxP recombination sites) bringing different elements of the sensitizing gene expression system together in a operable linkage such that the operable linkage results in the expression of the p53 gene (e.g., see abstract; Figure 9; column 2, lines 8-45; column 4, line 54 through column 8; column 16, line 1 through column 17 line 52), which would readily be recognized by one of ordinary skill in the art as a gene that has the potential to cause tumor cells to be killed. It is noted that claims 44-46 encompass a kit which may comprise instructions for use of the vector(s) in antitumor therapy. Kit and instructions are not considered critical limitations that have patentable weight. Furthermore, instructions "for use of the vector(s) in antitumor therapy" is a functional limitation. As such, the rejection of the kit claims as being anticipated by Graham are appropriate.

Conclusion

No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (571) 272-0756. The examiner can normally be reached on M-F (8:00-5:30) with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1635

DAVE T. NGUYEN
PRIMARY EXAMINER